REMARKS

Status of the Claims

Claims 1-74 are currently pending. Claims 31-74 were withdrawn from consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention. Claims 1-30 were examined and rejected.

In this amendment, claim 29 has been canceled without prejudice or disclaimer, and claims 1, 3, 6, 7, 22 and 25 have been amended to correct typographical errors and claim dependencies and to clarify the invention. No new matter has been added. Upon entry of this amendment, claims 1-28 and 30-74 will be pending, of which claims 1-28 and 30 are subject to further examination. Entry of the amendment and reconsideration in view of the following comments is respectfully requested.

With respect to all amendments, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Rejection under 35 U.S.C. § 101, Double-Patenting

Claims 1-22 and 30 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-23 of co-pending U.S. Patent Application Serial No. 10/556,182, as set forth in detail on pages 3-4 of the OA.

Applicants elect to hold this matter in abeyance until such time as the claims are allowed.

Rejection under 35 U.S.C. § 112, Second Paragraph

Claims 6-7, both of which depend from claim 2, are rejected under 35 U.S.C. § 112, ¶ 2 because they recite the limitations "the conserved region", "the structural protein", "the non-structural protein", and "the variable region" without proper antecedent basis in claim 2.

Claims 6 and 7 have been amended to change their claim dependencies to claims 5 and 3, respectively, thereby rendering this rejection moot. Accordingly, it is respectfully submitted that this rejection under 35 U.S.C. § 112, ¶ 2 may be withdrawn.

Claim Objection

Claim 22 is objected to because of the recitation of "a respiratory sncytical virus". This objection is rendered moot by the amendment of claim 22.

Rejections under 35 U.S.C. § 102

Anticipation by Fodor

Claims 1-8, 21 and 30 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Fodor *et al.* (US 6,355,432, hereinafter "Fodor").

The Office alleges that Fodor discloses the limitations of independent claim 1 by teaching a process capable of producing a matrix having each of the different possible 10-mer oligonucleotides (col. 19, lines 42-66) and therefore *inherently* comprising each of the presently claimed oligonucleotide probes. Applicants respectfully traverse this rejection for the reasons set forth below.

The legal standard for anticipation under 35 U.S.C. § 102 is one of strict identity. *Trintec Industries, Inc. v. Top-U.S.A. Corp.*, 63 U.S.P.Q.2d 1597 (Fed. Cir. 2002). To anticipate a claim, a single prior source must contain each and every limitation of the claimed invention. *In re Paulson*,

30 F.3d 1475, 1478-79, 31 USPQ2d 1671, 1673 (Fed. Cir. 1994) (*citing In re Spada*, 911 F.2d 705, 708, 15 USPQ2 d 1655, 1657 (Fed. Cir. 1990)). "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); MPEP § 2131.

Fodor teaches methods and apparatus for sequencing, fingerprinting and mapping biological macromolecules, typically biological polymers (abstract). The passage cited by the Office states:

> The production of the collection of specific oligonucleotides used in polynucleotide sequencing may be produced in at least two different ways. Present technology certainly allows production of ten nucleotide oligomers on a solid phase or other synthesizing system. See, e.g., instrumentation provided by Applied Biosystems, Foster City, Calif. Although a single oligonucleotide can be relatively easily made, a large collection of them would typically require a fairly large amount of time and investment. For example, there are 4^{10}=1,048,576 possible ten nucleotide oligomers. Present technology allows making each and everyone of them in a separate purified form though such might be costly and laborious.
>
> Once the desired repertoire of possible oligomer sequences of a given length have been synthesized, this collection of reagents may be individually positionally attached to a substrate, thereby allowing a batchwise hybridization step. Present technology also would allow the possibility of attaching each and everyone of these 10-mers to a separate specific position on a solid matrix. This attachment could be automated in any of a number of ways, particularly through the use of a caged biotin type linking. This would produce a matrix having each of different possible 10-mers. (Emphasis added).

Thus, Fodor is a biological tool patent. It does not teach any SARS or non-SARS specific oligonucleotides; nor does it teach any specific oligonucleotide sequences at all. All it teaches is a new method of attaching any string of nucleic acids to a separate specific position on a solid matrix. In patent terms, Fodor broadly discloses a genus of 10-mer oligonucleotides that encompasses over a million distinct species.

It is well settled that a genus does not always anticipate a claim to a species within the genus. MPEP § 2131.02 (emphasis added). When the compound is not specifically named, but instead it is necessary to select portions of teachings within a reference and combine them, e.g., select various substituents from a list of alternatives given for placement at specific sites on a generic chemical formula to arrive at a specific composition, anticipation can only be found if the classes of substituents are sufficiently limited or well delineated. *Ex parte A*, 17 USPQ2d 1716 (B.P.A.I. 1990) (emphasis added). If one of ordinary skill in the art is able to "at once envisage" the specific compound within the generic chemical formula, the compound is anticipated. One of ordinary skill in the art must be able to draw the structural formula or write the name of each of the compounds included in the generic formula before any of the compounds can be "at once envisaged." One may look to the preferred embodiments to determine which compounds can be anticipated. *In re Petering*, 301 F.2d 676, 133 USPQ 275 (CCPA 1962) (emphasis added).

In *In re Petering*, the prior art disclosed a generic chemical formula "wherein X, Y, Z, P, and R"- represent either hydrogen or alkyl radicals, R a side chain containing an OH group." The court held that this formula, without more, could not anticipate a claim to 7-methyl-9-[d, l"-ribityl]-isoalloxazine because the generic formula encompassed a vast number and perhaps even an infinite number of compounds. MPEP § 2131.02 (emphasis added).

Much like the prior art in *In re Petering*, Fodor merely discloses a genus encompassing a vast number ($> 10^6$) of oligonucleotides having a general formula of $(A/T/G/C)_{10}$ without providing any further guidance whatsoever with respect to SARS and/or non-SARS diagnostics. Based on the teachings of Fodor, a person skilled in the art could not possibly "at once envisage" the presently claimed oligonucleotide sequences because the person skilled in the art would not be able "to draw the structural formula or write the name of each of the compounds." Accordingly, much like the generic formula in *In re Petering* could not anticipate the claimed 7-methyl-9-[d, l"-ribityl]-isoalloxazine compound, the enormous genus of 10-mer oligonucleotides taught by Fodor cannot possibly anticipate the presently claimed SARS-CoV and non-SARS-CoV oligonucleotide probes. If the opposite were true, any DNA or polypeptide synthesis method patent would effectively

preclude all patents on genes or proteins, respectively, by teaching how to prepare a sequence of nucleotides or amino acids of every conceivable order and length. This, of course, is not the case.

Claim 1 recites a diagnostic chip that is capable of detecting a SARS and non-SARS infection. In order to anticipate a claim to a diagnostic chip, it is not enough to disclose an array comprising millions of oligonucleotide probes. For the array to have any diagnostic value, it is also necessary to match oligonucleotide probes with specific pathogenic organisms and/or pathological conditions. Fodor was filed on June 2, 2000, claiming the earliest priority date of June 7, 1989, and issued on March 12, 2002. The first instance of SARS was reported in November 2002, and the SARS coronavirus (SARS-CoV) was not identified until April 2003. The full genome sequence of the SARS-CoV was first published in May 2003. Thus, the logical link between SARS-CoV oligonucleotide probes and SARS simply did not exist when the Fodor patent issued.

The Office seems to take the position that Fodor *inherently* anticipates the present invention even in the absence of the logical link between the oligonucleotide probes and SARS. Applicants respectfully submit that the law of inherent anticipation does not extend so far as to vitiate the common principles of genus-species anticipation discussed above. "An invitation to investigate is not an inherent disclosure" where a prior art reference "discloses no more than a broad genus of potential applications of its discoveries." MPEP § 2112, citing *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1367, 71 USPQ2d 1081, 1091 (Fed. Cir. 2004) (emphasis added). "A prior art reference that discloses a genus still does not inherently disclose all species within that broad category" but must be examined to see if a disclosure of the claimed species has been made or whether the prior art reference merely invites further experimentation to find the species. *Id.* (emphasis added). In this case, Fodor does not provide any teachings whatsoever that would enable a person skilled in the art to practice the present invention.

In light of the foregoing discussion, Fodor does not teach each and every element of the present invention and therefore does not constitute an anticipating prior art reference. Accordingly, it is respectfully submitted that this rejection under 35 U.S.C. § 102(b) may properly be withdrawn.

Anticipation by Shi as Evidenced by Marra

Claims 1-8, 15, 21 and 30 are rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Shi *et al.* (*Chin. Sci. Bull.* 2003, 48(12):1165-1169, referred to in the OA as "Rong", which is actually the primary author's first name; hereinafter "Shi") as evidenced by Marra *et al.* (*Science* 2003, 300:1399-1404, hereinafter "Marra").

Shi allegedly teaches an oligonucleotide microarray for SARS-CoV detection. Marra allegedly teaches the complete SARS-CoV genome. Applicants respectfully traverse this rejection for the reasons set forth below.

As an initial matter, Claim 1 as amended no longer recites an oligonucleotide probe complementary to a nucleotide sequence of a non-SARS-CoV coronaviridae virus. Since claims 1-8, 15, 21 and 30 depend, directly or indirectly, from claim 1, they all incorporate all of the limitations of claim 1.

Shi teaches a nucleotide array for detecting SARS-CoV comprising 30 specific 60-mer oligonucleotides designed to cover the entire genome of the first submitted SARS-CoV strain (GeneBank Accession No. AY274110) (abstract). Shi further teaches that oligo 10 in Table 1 is a common sequence of SARS-CoV, bovine coronavirus, murine hepatitis virus, rat coronavirus and avian infectious bronchitis virus (page 1167, Table 1). Marra teaches that some of the oligonucleotides disclosed in Table 1 of Shi correspond to the Replicase 1A and Spike glycoprotein (S-gene) regions of the SARS-CoV genome. Each of the non-SARS-CoV organisms taught in Shi belongs to the category non-SARS-CoV coronaviridae viruses, which is no longer recited in claim 1 as amended. Therefore, Shi does not teach a SARS diagnostic chip comprising one or more oligonucleotide probe(s) complementary to a nucleotide sequence of any of the non-SARS-CoV infectious organisms recited in claim 1 as amended.

Since Shi does not teach a SARS diagnostic chip comprising one or more oligonucleotide probe(s) complementary to a nucleotide sequence of any of the non-SARS-CoV infectious

organisms recited in claim 1 as amended, Shi does not teach each and every element of the present invention and therefore does not meet the strict identity standard for anticipation. Accordingly, Applicants respectfully submit that this rejection under 35 U.S.C. § 102(a) may be withdrawn.

Rejections under 35 U.S.C. § 103

Fodor in View of Ruan

Claims 9 and 10 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Fodor as applied to claims 1-8, 21 and 30 above and further in view of Ruan *et al.* (*The Lancet* 2003, 361(9371):1779-85, hereinafter "Ruan").

The teachings of Fodor have been discussed in detail above. The Office acknowledges that Fodor does not explicitly teach the sequence of SEQ ID NO:210 (which corresponds to a SARS-CoV Replicase oligonucleotide probe PBS00024). To cure this deficiency, the Office cites Ruan, which allegedly teaches a nucleotide sequence comprising a region having 100% identity with SEQ ID NO:210. The Office argues that it would have been *prima facie* obvious to a person skilled in the art at the time of the invention to combine the teachings of Fodor and Ruan to arrive at the presently claimed invention. Applicants respectfully traverse this rejection for the reasons set forth below.

The obviousness analysis under 35 U.S.C. § 103(a) requires the consideration of the scope and content of the prior art, the level of skill in the relevant art, and the differences between the prior art and the claimed subject matter must be considered. *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727 (2007) (*citing Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966)). To establish a prima facie case of obviousness a three-prong test must be met. First, the prior art must reference must teach or suggest all the claim limitations. *In re Royka*, 490 F.2d 981, 985 (CCPA 1974). Second, there must be some suggestion or motivation, either in the references or in the knowledge generally available among those of ordinary skill in the art, to modify the reference to achieve the claimed invention.

KSR at 1731. And third, there must be a reasonable expectation of success found in the prior art. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

The relevant teachings of Fodor are discussed in detail above. The main problem with Fodor is that it discloses a very large ($>10^6$) genus of oligonucleotides of a general formula $(A/T/G/C)_{10}$ but does not teach any specific nucleotide sequences, SARS-CoV or non-SARS-CoV. Furthermore, Fodor does not provide any guidance whatsoever that would lead a person skilled in the art to choose the particular oligonucleotide probes recited in the present claims. Additionally, as discussed above, the existence of SARS-CoV was not even known at the time of Fodor's issuance.

The fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness. MPEP § 2144.08, citing *In re Baird*, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994) ("The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious."); *In re Jones*, 958 F.2d 347, 350, 21 USPQ2d 1941, 1943 (Fed. Cir. 1992) (Federal Circuit has "decline[d] to extract from *Merck* [*& Co. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir. 1989)] the rule that... regardless of how broad, a disclosure of a chemical genus renders obvious any species that happens to fall within it."). To establish a *prima facie* case of obviousness in a genus-species situation such as this, the Office needs to consider a number of factors including, *inter alia*, the size of the genus, the structural similarity, the teachings of similar properties or uses, and so forth. *See* MPEP § 2144.08.

Additionally, obviousness cannot be predicated on what is not known at the time an invention is made, even if the inherency of a certain feature is later established. MPEP § 2141.02; *In re Rijckaert*, 9 F.2d 1531, 28 USPQ2d 1955 (Fed. Cir. 1993) (emphasis added). "[T]he inherency of an advantage and its obviousness are entirely different questions[;] [t]hat which may be inherent is not necessarily known[;] [o]bviousness cannot be predicated on what is unknown." *In re Spormann*, 363 F.2d 444, 448; 150 USPQ 449 (CCPA 1966). Thus, inherency may not serve as a substitute for a motivation to modify or combine the teachings of prior art, or for a reasonable expectation of success.

In this case, the genus of 10-mer oligonucleotide probes is very large and diverse; the structural similarity is low; and the prior art does not teach similar properties or uses with respect to SARS diagnostics. Moreover, as discussed above, SARS-CoV had not even been discovered at the time of Fodor's issuance. Under this particular set of facts, it is apparent that the combination of Fodor and Ruan does not teach or even suggest a diagnostic chip featuring all the limitations recited in claims 9 and 10. In the absence of a teaching or suggestion of each and every claim element, the cited combination fails to provide the motivation to practice the presently claimed invention with a reasonable expectation of success.

Thus, it is respectfully submitted that the Office has failed to establish a *prima facie* case of obviousness, and therefore this rejection under 35 U.S.C. § 103(a) may properly be withdrawn.

Fodor in View of Briese

Claims 11 and 12 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Fodor as applied to claims 1-8, 21 and 30 above and further in view of Briese *et al.* (U.S. Pub. No. 2004/0265796, hereinafter "Briese").

The teachings of Fodor have been discussed in detail above. The Office acknowledges that Fodor does not explicitly teach the sequence of SEQ ID NO:225 (which corresponds to a SARS-CoV N-gene oligonucleotide probe PBS00040). To cure this deficiency, the Office cites Briese, which allegedly teaches a nucleotide sequence comprising a region having 100% identity with SEQ ID NO:225. The Office argues that it would have been *prima facie* obvious to a person skilled in the art at the time of the invention to combine the teachings of Fodor and Briese to arrive at the presently claimed invention.

The combination of Fodor and Briese does not render claims 11 and 12 obvious for substantially the same reasons as those set forth above with respect to Fodor and Ruan. Namely, the combination of Fodor and Briese does not teach or even suggest a diagnostic chip featuring all the limitations recited in claims 11 and 12. In the absence of a teaching or suggestion of each and every

claim element, the cited combination fails to provide the motivation to practice the presently claimed invention with a reasonable expectation of success.

Thus, it is respectfully submitted that the Office has failed to establish a *prima facie* case of obviousness, and therefore this rejection under 35 U.S.C. § 103(a) may properly be withdrawn.

Fodor in View of Vilalta

Claims 13 and 14 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Fodor as applied to claims 1-8, 21 and 30 above and further in view of Vilalta *et al.* (WO 2005021707: March 2005, hereinafter "Vilalta").

The teachings of Fodor have been discussed in detail above. The Office acknowledges that Fodor does not explicitly teach the sequence of SEQ ID NO:229 (which corresponds to a SARS-CoV S-gene oligonucleotide probe PBS00044). To cure this deficiency, the Office cites Vilalta, which allegedly teaches a nucleotide sequence comprising a region having 100% identity with SEQ ID NO:229. The Office argues that it would have been *prima facie* obvious to a person skilled in the art at the time of the invention to combine the teachings of Fodor and Vilalta to arrive at the presently claimed invention.

The combination of Fodor and Vilalta does not render claims 13 and 14 obvious for substantially the same reasons as those set forth above with respect to Fodor and Ruan. Namely, the combination of Fodor and Vilalta does not teach or even suggest a diagnostic chip featuring all the limitations recited in claims 13 and 14. In the absence of a teaching or suggestion of each and every claim element, the cited combination fails to provide the motivation to practice the presently claimed invention with a reasonable expectation of success.

Thus, it is respectfully submitted that the Office has failed to establish a *prima facie* case of obviousness, and therefore this rejection under 35 U.S.C. § 103(a) may properly be withdrawn.

Fodor in View of Martoglio

Claims 16-19 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Fodor as applied to claims 1-8, 21 and 30 above and further in view of Martoglio *et al.* (*Mol. Med.* 2000, 6(9):750-765, hereinafter "Martoglio").

The teachings of Fodor have been discussed in detail above. Regarding claims 16 and 17, the Office acknowledges that Fodor does not teach the spiking of a non-SARS-CoV sequence in the sample, and also does not teach that the sequence is of *Arabidopsis* origin. Regarding claims 18 and 19, the Office acknowledges that Fodor does not teach the inclusion of an immobilization control probe or a positive control probe. To cure these deficiencies, the Office cites Martoglio, which allegedly teaches the inclusion of these probes in a microarray format, and argues that it would have been *prima facie* obvious to a person skilled in the art at the time of the invention to combine the teachings of Fodor and Martoglio to arrive at the presently claimed invention.

The combination of Fodor and Martoglio does not render claims 16-19 obvious for substantially the same reasons as those set forth above with respect to Fodor and Ruan. Namely, the combination of Fodor and Martoglio does not teach or even suggest a diagnostic chip featuring all the limitations recited in claims 16-19. In the absence of a teaching or suggestion of each and every claim element, the cited combination fails to provide the motivation to practice the presently claimed invention with a reasonable expectation of success.

Thus, it is respectfully submitted that the Office has failed to establish a *prima facie* case of obviousness, and therefore this rejection under 35 U.S.C. § 103(a) may properly be withdrawn.

Fodor in View of Saiki

Claim 20 is rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Fodor as applied to claims 1-8, 21 and 30 above and further in view of Saiki *et al.* (*P.N.A.S.* 1989, 86:6230-6234, hereinafter "Saiki").

The teachings of Fodor have been discussed in detail above. Saiki allegedly teaches an embodiment wherein at least one of the oligonucleotide probe comprises, at its 5' end, a poly dl' region to enhance its immobilization on the support. The Office argues that it would have been *prima facie* obvious to a person skilled in the art at the time of the invention to combine the teachings of Fodor and Saiki to arrive at the presently claimed invention.

The combination of Fodor and Saiki does not render claim 20 obvious for substantially the same reasons as those set forth above with respect to Fodor and Ruan. Namely, the combination of Fodor and Saiki does not teach or even suggest a diagnostic chip featuring all the limitations recited in claim 20. In the absence of a teaching or suggestion of each and every claim element, the cited combination fails to provide the motivation to practice the presently claimed invention with a reasonable expectation of success.

Thus, it is respectfully submitted that the Office has failed to establish a *prima facie* case of obviousness, and therefore this rejection under 35 U.S.C. § 103(a) may properly be withdrawn.

Fodor in View of Marra

Claims 22-29 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Fodor as applied to claims 1-8, 21 and 30 above and further in view of Marra.

The teachings of Fodor have been discussed in detail above. With regard to claims 22 and 23, Marra allegedly teaches an embodiment wherein the non-SARS-CoV infectious organism causing SARS-like symptoms is a human coronavirus (Figure 1, legend). With regard to claims 24-29, Marra allegedly teaches that a variety of additional viruses and organisms are listed as related to SARS-CoV phylogenetically. (*Id.*) The Office argues that it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have extended the teachings of Fodor to include the additional non-SARS-CoV infectious organisms disclosed by Marra to arrive at the claimed invention with a reasonable expectation for success. The Office then makes presumably unintentional references to the teachings of Shi, and essentially argues that one of ordinary skill in

the art at the time of the invention would have been motivated to have extended the teachings of Fodor to include the additional non-SARS-CoV infectious organisms disclosed by Marra to arrive at the claimed invention with a reasonable expectation for success.

As an initial matter, this rejection is moot with respect to canceled claim 29. With respect to claims 22-28, Applicants respectfully traverse this rejection for the reasons set forth below.

The combination of Fodor and Marra does not render claims 22-28 obvious for substantially the same reasons as those set forth above with respect to Fodor and Ruan. Namely, the combination of Fodor and Marra does not teach or even suggest a diagnostic chip featuring all the limitations recited in claims 22-28. In the absence of a teaching or suggestion of each and every claim element, the cited combination fails to provide the motivation to practice the presently claimed invention with a reasonable expectation of success. Moreover, Applicants fail to see how different infectious organisms' being grouped together in a phylogenetic tree can provide a motivation to combine oligonucleotides complementary to nucleotide sequences of any of these organisms on the same diagnostic chip with a reasonable expectation of success.

Thus, it is respectfully submitted that the Office has failed to establish a *prima facie* case of obviousness, and therefore this rejection under 35 U.S.C. § 103(a) may properly be withdrawn.

Shi in View of Ruan

Claims 9 and 10 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Shi as applied to claims 1-8, 15, 21 and 29-30 above and further in view of Ruan.

The teachings of Shi have been discussed in detail above. The Office acknowledges that Shi does not explicitly teach the sequence of SEQ ID NO:210 (which corresponds to a SARS-CoV Replicase oligonucleotide probe PBS00024). To cure this deficiency, the Office cites Ruan, which allegedly teaches a nucleotide sequence comprising a region having 100% identity with SEQ ID NO:210. The Office argues that it would have been *prima facie* obvious to a person skilled in the art

at the time of the invention to combine the teachings of Shi and Ruan to arrive at the presently claimed invention.

As discussed above, claim 1 as amended no longer recites an oligonucleotide probe complementary to a nucleotide sequence of a non-SARS-CoV coronaviridae virus. Since claims 9 and 10 depend, directly or indirectly, from claim 1, they all incorporate all of the limitations of claim 1. Accordingly, Shi does not teach a SARS diagnostic chip comprising one or more oligonucleotide probe(s) complementary to a nucleotide sequence of any of the non-SARS-CoV infectious organisms recited in claim 1 as amended.

Since Ruan does not contain any teachings that would remedy this deficiency of Shi, it is apparent that the combination of Shi and Ruan does not teach or even suggest a diagnostic chip featuring all the limitations recited in claims 9 and 10. In the absence of a teaching or suggestion of each and every claim element, the cited combination fails to provide the motivation to practice the presently claimed invention with a reasonable expectation of success.

Thus, it is respectfully submitted that the Office has failed to establish a *prima facie* case of obviousness, and therefore this rejection under 35 U.S.C. § 103(a) may properly be withdrawn.

Shi in View of Briese

Claims 11 and 12 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Shi as applied to claims 1-8, 15, 21 and 29-30 above and further in view of Briese.

The teachings of Shi have been discussed in detail above. The Office acknowledges that Shi does not explicitly teach the sequence of SEQ ID NO:225 (which corresponds to a SARS-CoV N-gene oligonucleotide probe PBS00040). To cure this deficiency, the Office cites Briese, which allegedly teaches a nucleotide sequence comprising a region having 100% identity with SEQ ID NO:225. The Office argues that it would have been *prima facie* obvious to a person skilled in the art

at the time of the invention to combine the teachings of Shi and Briese to arrive at the presently claimed invention.

The combination of Shi and Briese does not render claims 11 and 12 obvious for substantially the same reasons as those set forth above with respect to Shi and Ruan. Namely, the combination of Shi and Briese does not teach or even suggest a diagnostic chip featuring all the limitations recited in claims 11 and 12. In the absence of a teaching or suggestion of each and every claim element, the cited combination fails to provide the motivation to practice the presently claimed invention with a reasonable expectation of success.

Thus, it is respectfully submitted that the Office has failed to establish a *prima facie* case of obviousness, and therefore this rejection under 35 U.S.C. § 103(a) may properly be withdrawn.

Shi in View of Vilalta

Claims 13 and 14 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Shi as applied to claims 1-8, 15, 21 and 29-30 above and further in view of Vilalta.

The teachings of Shi have been discussed in detail above. The Office acknowledges that Shi does not explicitly teach the sequence of SEQ ID NO:229 (which corresponds to a SARS-CoV S-gene oligonucleotide probe PBS00044). To cure this deficiency, the Office cites Vilalta, which allegedly teaches a nucleotide sequence comprising a region having 100% identity with SEQ ID NO:229. The Office argues that it would have been *prima facie* obvious to a person skilled in the art at the time of the invention to combine the teachings of Shi and Vilalta to arrive at the presently claimed invention.

The combination of Shi and Vilalta does not render claims 13 and 14 obvious for substantially the same reasons as those set forth above with respect to Shi and Ruan. Namely, the combination of Shi and Vilalta does not teach or even suggest a diagnostic chip featuring all the limitations recited in claims 13 and 14. In the absence of a teaching or suggestion of each and every

claim element, the cited combination fails to provide the motivation to practice the presently claimed invention with a reasonable expectation of success.

Thus, it is respectfully submitted that the Office has failed to establish a *prima facie* case of obviousness, and therefore this rejection under 35 U.S.C. § 103(a) may properly be withdrawn.

Shi in View of Martoglio

Claims 16-19 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Shi as applied to claims 1-8, 15, 21 and 29-30 above and further in view of Martoglio.

The teachings of Shi have been discussed in detail above. Regarding claims 16 and 17, the Office acknowledges that Shi does not teach the spiking of a non-SARS-CoV sequence in the sample, and also does not teach that the sequence is of *Arabidopsis* origin. Regarding claims 18 and 19, the Office acknowledges that Shi does not teach the inclusion of an immobilization control probe or a positive control probe. To cure these deficiencies, the Office cites Martoglio, which allegedly teaches the inclusion of these probes in a microarray format, and argues that it would have been *prima facie* obvious to a person skilled in the art at the time of the invention to combine the teachings of Shi and Martoglio to arrive at the presently claimed invention.

The combination of Shi and Martoglio does not render claims 16-19 obvious for substantially the same reasons as those set forth above with respect to Shi and Ruan. Namely, the combination of Shi and Martoglio does not teach or even suggest a diagnostic chip featuring all the limitations recited in claims 16-19. In the absence of a teaching or suggestion of each and every claim element, the cited combination fails to provide the motivation to practice the presently claimed invention with a reasonable expectation of success.

Thus, it is respectfully submitted that the Office has failed to establish a *prima facie* case of obviousness, and therefore this rejection under 35 U.S.C. § 103(a) may properly be withdrawn.

Shi in View of Saiki

Claim 20 is rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Shi as applied to claims 1-8, 21 and 29-30 above and further in view of Saiki.

The teachings of Shi have been discussed in detail above. Saiki allegedly teaches an embodiment wherein at least one of the oligonucleotide probe comprises, at its 5' end, a poly dI' region to enhance its immobilization on the support. The Office argues that it would have been *prima facie* obvious to a person skilled in the art at the time of the invention to combine the teachings of Shi and Saiki to arrive at the presently claimed invention.

The combination of Shi and Saiki does not render claim 20 obvious for substantially the same reasons as those set forth above with respect to Shi and Ruan. Namely, the combination of Shi and Saiki does not teach or even suggest a diagnostic chip featuring all the limitations recited in claim 20. In the absence of a teaching or suggestion of each and every claim element, the cited combination fails to provide the motivation to practice the presently claimed invention with a reasonable expectation of success.

Thus, it is respectfully submitted that the Office has failed to establish a *prima facie* case of obviousness, and therefore this rejection under 35 U.S.C. § 103(a) may properly be withdrawn.

Shi in View of Marra

Claims 22-28 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Shi as applied to claims 1-8, 15, 21 and 29-30 above and further in view of Marra.

The teachings of Shi have been discussed in detail above. With regard to claims 22 and 23, Marra allegedly teaches an embodiment wherein the non-SARS-CoV infectious organism causing SARS-like symptoms is a human coronavirus (Figure 1, legend). With regard to claims 24-28, Marra allegedly teaches that a variety of additional viruses and organisms are listed as related to SARS-CoV phylogenetically. (*Id.*) The Office argues that it would have been *prima facie* obvious

to one of ordinary skill in the art at the time of the invention to have extended the teachings of Shi to include the additional non-SARS-CoV infectious organisms disclosed by Marra to arrive at the claimed invention with a reasonable expectation for success. The Office argues that Marra "does establish the phylogenetic relationship between the SARS-CoV genome, and particular coding features within the genome as compared to these non-SARS-CoV sequences." Since Shi already includes a probe complementary to a non-SARS-CoV sequence, the Office concludes that one of ordinary skill in the art at the time of the invention would have been motivated to have extended the teachings of Shi to include the additional non-SARS-CoV infectious organisms disclosed by Marra to arrive at the claimed invention with a reasonable expectation for success.

The combination of Shi and Marra does not render claims 22-28 obvious for substantially the same reasons as those set forth above with respect to Shi and Ruan. Namely, the combination of Shi and Marra does not teach or even suggest a diagnostic chip featuring all the limitations recited in claims 22-28. Additionally, despite the Office's assertion that it would have been obvious to one of ordinary skill in the art at the time of the invention "to have extended the teachings of Shi to include the additional non-SARS-CoV infectious organisms disclosed by Marra," Shi does not teach the idea of combining SARS-CoV and non-SARS-CoV diagnostics on one chip. Shi merely teaches that oligo 10 in Table 1 is a common sequence of SARS-CoV, bovine coronavirus, murine hepatitis virus, rat coronavirus and avian infectious bronchitis virus. Thus, it would be impossible to distinguish a SARS-CoV infection from a non-SARS-CoV infection using the diagnostic array of Shi. Since Shi does not teach the idea of distinguishing SARS-CoV from non-SARS-CoV infections, Shi contains no teachings whatsoever that could reasonably be "extended" by including the additional non-SARS-CoV infectious organisms of Marra. Moreover, Applicants fail to see how being grouped together in a phylogenetic tree can provide a motivation to combine oligonucleotides complementary to nucleotide sequences of different infectious organisms on the same diagnostic chip with a reasonable expectation of success.

Thus, it is respectfully submitted that the Office has failed to establish a *prima facie* case of obviousness, and therefore this rejection under 35 U.S.C. § 103(a) may properly be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing **docket No. 514572002000**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: November 10, 2008

Respectfully submitted,

Electronic signature: /Yan Leychkis/
Yan Leychkis
Registration No.: 60,440
MORRISON & FOERSTER LLP
12531 High Bluff Drive, Suite 100
San Diego, California 92130-2040
(858) 314-7702